Clinical and patient-reported outcomes of implants placed in autogenous bone grafts and implants placed in native bone: A case-control study with a follow-up of 5-16 years

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Abstract: AIMS To compare the radiographic marginal bone levels of implants placed in sites previously augmented with autogenous bone grafts and implants placed in native bone. Secondary outcomes included: implant survival, periodontal/peri-implant parameters as well as short- and long-term patient-reported outcome measures. MATERIALS AND METHODS The study was designed as a case-control study including 38 patients equally distributed into two groups (previously augmented with autogenous bone blocks [AB] and implants placed in native bone [NB]). In total, 67 implants were placed. Clinical, radiographic and patient-reported outcome measures (PROMs), and complication rates were assessed based on a chart review and at a follow-up examination (≥5 years after implant placement). Nonparametric mixed models were applied for the comparison of the two groups because of the clustered data. The data were analyzed descriptively, and p-values were calculated using nonparametric mixed models to account for the clustered data. RESULTS The mean follow-up time was 10.2 years (range 6-13 years; AB) and 8.3 years (range 5-16 years; NB). One implant was lost in group NB (97.5% survival rate) and none in group AB (100%). Following primary augmentation, six major complications (wound dehiscences, acute pulpitis, intra- and extraoral sensitivity disturbances) were observed at the donor sites. At time of implant placement, only minimal complications occurred and only in group NB. Median marginal bone levels at the follow-up were significantly higher in group NB (1.15; Q1: 0.50 mm/Q3: 1.83 mm) than in group AB (1.58; Q1: 1.01 mm/Q3: 2.40 mm; p = 0.0411). Probing depth, bleeding on probing and recession values were similar in both groups. PROMs revealed high visual analog scale values (i.e., high satisfaction) for both procedures. CONCLUSIONS Dental implants placed in sites augmented with autogenous bone or in native bone revealed healthy peri-implant tissues after 5-16 years. Marginal bone levels were significantly higher for implant placed in native bone. Complications following primary augmentation encompassed every third patient but were mostly transient.

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Clinical and patient-reported outcomes of implants placed in autogenous bone grafts and implants placed in native bone: a case-control study with a follow up of 5 to 16 years

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Abstract

Aims: to compare the radiographic marginal bone levels of implants placed in sites previously augmented with autogenous bone grafts and implants placed in native bone. Secondary outcomes included: implant survival, periodontal/peri-implant parameters as well as short- and long-term patient-reported outcome measures.

Materials and methods: The study was designed as a case-control study including 38 patients equally distributed into two groups (previously augmented with autogenous bone blocks (AB) and implants placed in native bone (NB)). In total 67 implants were placed. Clinical, radiographic and patient-reported outcome measures (PROMs) as well as complication rates were assessed based on a chart review and at a follow-up examination (≧5 years after implant placement). Nonparametric mixed models were applied for the comparison of the two groups because of the clustered data. The data was analyzed descriptively, and p-values were calculated using nonparametric mixed models to account for the clustered data.

Results: The mean follow-up time was 10.2 years (range 6-13 years; AB) and 8.3 years (range 5-16 years; NB). One implant was lost in group NB (97.5% survival rate) and none in group AB (100%). Following primary augmentation, six major complications (wound dehiscences, acute pulpitis, intra- and extraoral sensitivity disturbances) were observed at the donor sites. At time of implant placement, only minimal complications occurred and only in group NB. Median marginal bone levels at the follow-up were significantly higher in group NB (1.15; Q1: 0.50 mm/Q3: 1.83 mm) than in group AB (1.58; Q1: 1.01 mm/Q3: 2.40 mm; p=0.0411). Probing depth, bleeding on probing and recession values were similar in both groups. PROMs revealed high visual analogue scale values (i.e. high satisfaction) for both procedures.

Conclusions: Dental implants placed in sites augmented with autogenous bone or in native bone revealed healthy peri-implant tissues after 5-16 years. Marginal bone levels were significantly higher for implant placed in native bone. Complications following primary augmentation encompassed every third patient but were mostly transient.

Introduction

Dental implants demonstrate predictable long-term outcomes with high survival rates when placed in sufficient bone volume with an adequate bone quality (Adell et al., 1981, Pylant et al., 1992, Jemt and Lekholm, 1993, Weber et al., 2000). Due to the successful use of dental implants, treatment options have expanded over the years, starting as anchors for fixed reconstructions in fully edentulous cases to single implants supporting crowns in the esthetic zone.

Clinically, a prosthetically-driven implant planning may result in a prospective implant location that does not present a sufficient bone volume to place a dental implant. This is due to an atrophy of hard and soft tissues following tooth loss (Amler et al., 1960, Pietrokovski and Massler, 1967). In case the amount of bone volume is not sufficient to achieve primary implant stability, various options exist to augment bone at the desired site prior to implant placement (Raghoebar et al., 2007). Among the methods described in the literature, the use of autogenous bone blocks is considered as gold standard (Stern and Barzani, 2015).

Autogenous bone grafts provide an excellent biologic compatibility, are predictable and render sufficient bone quality and quantity to place dental implants (Raghoebar et al., 2007, Von Arx and Buser, 2006). Extra- and intraoral donor sites may be considered to harvest the desired bone grafts. Extraoral donor sites necessitate extensive surgery and hospitalization of the patient increasing the costs of the treatment and the morbidity of the patient (Marx and Morales, 1988). If the volume of the required bone is not larger than a three-teeth segment, intraoral sites may be preferred over extraoral sites (Raghoebar et al., 2007). As intraoral donor sites, the chin region, the posterior regions of the mandible or the tuberositas in the maxilla may be considered (Zeltner et al., 2016). The closer the donor and recipient sites are, the shorter is the opening flap, the surgery and anesthesia time (Misch, 1997). The access to harvest a chin bone graft was reported to be easily accessible and convenient, the type and quality of bone obtainable to be sufficient, and the risk-benefit ratio to be excellent (Raghoebar et al., 2007). Due to that, the harvesting of chin bone has been extensively described in the literature (Hoppenreijs et al., 1992, Misch et al., 1992, Weibull et al., 2009, Nkenke et al., 2001). In contrast, bone harvested from the retromolar area shows less morbidity (Raghoebar et al., 2007). A couple of disadvantages and limitations

reported as patient morbidity at the donor site were described. This included: i) altered sensation, ii) sensory disturbance, iii) pain, iv) sensitivity loss of the lower anterior teeth and, v) recipient site morbidity such as resorption of the graft and intra-oral scarring (Weibull et al., 2009, Nkenke et al., 2001, Raghoebar et al., 2001, Clavero and Lundgren, 2003, Joshi, 2004).

While the efficacy of autogenous bone grafting procedures has been comprehensively described in the literature, only few data are available reporting on the long-term morbidity and on the long-term outcome of implants placed into previously augmented bone grafts.

The aims of the present study were i) to compare the long-term survival and clinical performance of implants placed in sites previously augmented with autogenous bone grafts and implants placed in native bone and ii) to report short- and long-term patient-reported outcome measures.

Materials and methods

Study design

The present study was designed as a case-control study. Prior to the start of the investigation, ethical approval was obtained (KEK-ZH-Nr. 2013-0429).

The electronic database of the Clinic of Fixed and Removable Prosthodontics and Dental Material Science, Center of Dental Medicine, University of Zurich was screened for potentially eligible patients having received an autogenous bone block graft between 2001 and 2007 (AB group). For the NB group, a pool of patients having received an implant in native bone with a follow-up of at least 5 years after implant placement was available. Nineteen patients per group were randomly selected for the follow-up examination. All patients included were asked to sign an informed consent. The follow-up visits took place between the January 2014 and June 2015. Patients unwilling to attend a follow-up examination and pregnant patients were excluded from the study. Altogether, 27 implants were placed in 19 patients in the test group and 40 implants were placed in 19 patients in the control group. All 67 placed implants were included in the statistical analysis.

Chart review

A chart review of the patients' history was performed. This included: demographic data (gender, age, smoking status), the date of surgery, the location of the receipt site (if applicable), materials used for bone augmentation (if applicable), the general wound healing after bone augmentation (if applicable), the time between the grafting procedure (if applicable) and implant placement, and if described any reported complications, the respective severity and if the therapy of these complications was successful.

Follow-up examination

Radiographic examination

Intraoral radiographs were taken using a paralleling technique with Rinn-holders (Super-Bite™, Kerr, Bioggio, Switzerland) and digital films. As the primary outcome, mesial and distal marginal bone levels (MBL) were calculated using an open-source software (Image J, National Institutes of

Health, Bethesda, Maryland USA). The radiographic distance between two implant threads was used to normalize for the magnification factor. The MBL was determined as the distance between the implant reference points (flat top of two-piece implants; implant shoulder minus 1.8mm for one-piece implants (this represents the transition between rough and smooth surface) and the first bone to implant contact (Gamper et al., 2017). Thereby, smaller values represent higher bone levels, i.e. the marginal bone level is closer to the implant shoulder (more favorable). All measurements were performed by the same blinded examiner not involved in any of the surgical and/or prosthetic procedures.

Clinical examination

As secondary parameters, the survival of the implants and general periodontal parameters were assessed including the two neighboring teeth. Recorded measurements were probing depth (PD) (Ramfjord, 1974), plaque control record (PCR) (O'Leary et al., 1972) bleeding on probing (BOP) (Ainamo and Bay, 1975), recession (REC) and the buccal width of the keratinized tissue (KT). All measurements except KT were recorded at 6 sites per tooth and implant (mesiobuccal, buccal, distobuccal, distolingual, lingual and mesiolingual) using a UNC-15 periodontal probe (Hu-Friedy, Chicago, IL, USA). The width of the KT was measured at the buccal aspect of all implants.
Additionally, general dental findings (sensitivity testing, sensation problems, changes of the morphology and the presence or absence of teeth) were recorded at sites adjacent to the implants and at the donor sites for the AB group.

Questionnaires

AB group

In order to assess patient-reported outcome measures (PROMs) regarding the donor/recipient site, a questionnaire with six specific questions was filled out by the patients. Question one and two related to any sensory problems (change over time) and adverse symptoms at the donor site. Question three related to adverse symptoms at the recipient site. Questions four to six were asked using a VAS (visual analog scale) ranging from 1 to 10. Question 4 related to the

perception of the surgical intervention. With question 5, patients were asked whether or not they would undergo the surgery for a second time. Question 6 asked whether or not patients would recommend the therapy to a family member.

NB group

A slightly modified questionnaire was handed to the patients in the NB group. The first two questions were excluded since no donor site was apparent in the NB group.

Statistical analysis

The sample size was calculated for parametric testing (Unpaired t-test) using the following link: http://biomath.info/power/ttest.htm. The assumptions for the primary outcome (radiographic marginal bone level changes) were 2 mm for the AB group, 1 mm for the NB group with a standard deviation of 1 mm (Dasmah et al., 2012). The computed sample size was 17 patients per group. A priori sample size calculation can only be performed for parametric testing, we were however expecting to obtain non-normally distributed data. To compensate we added 15% to obtain a final sample size of 19 per group.

All data were recorded in Microsoft Excel spreadsheets (Microsoft Corporation, Redmond, WA, USA). Statistical analysis was performed with SAS Version 9.4. The data was analyzed descriptively, and p-values were calculated using nonparametric mixed models to account for the clustered data (Brunner-Langer Analysis).

Results

Demographics and survival

Overall 38 subjects participated in the follow-up examination split in equally sized NB and AB groups with 19 patients (Table 1). The patients' age range was 30 to 92 years. The patients in the AB group had a mean age of 50 years (range: 30 – 76) and in the NB group of 72 years (57 – 92). Smoking habits were reported in the AB group only (two patients 5<10 cigarettes per day (Table 1)). There were no heavy smokers (>10cig/day) included in the study. According to Nitzan et al. (Nitzan et al., 2005) smoking as a strong confounding factor is therefore excluded.

Recipient site locations are displayed in Table 2. All autogenous bone blocks were applied in combination with a xenogeneic bone substitute material (Bio-Oss, Geistlich Biomaterials) and a xenogeneic native collagen membrane (Bio-Gide, Geistlich Biomaterials). Dental implants were placed after a mean healing time of 7 months (range 5-12 months).

The mean follow-up time after implant placement was 10 years (range 6-13 years) in the AB and 9 years (range 5-16 years) in the NB group.

The overall implant survival rate was 98.5%. One implant was lost in the NB group due to peri-implant disease (position 13). Hence, the survival rate for the AB group was 100% and for the NB group 97.5%

Chart review

Complications following primary augmentation (AB group only)

In six patients, complications were observed at the donor sites, but none at the receipt sites. The complications at the donor site were considered to be major (two wound dehiscences, one case with an acute pulpitis of three teeth, two sensitivity disturbances (extraorally decreased sensitivity) and one wound dehiscence combined with sensitivity disturbance (extraorally decreased sensitivity). One tooth with a pulpitis (in position 41) had to undergo root canal treatment. One patient had a sensitivity disturbance that slightly improved over time. All other complications were successfully treated (wound dehiscences) or healed without further therapy.

Complications following implant placement (AB and NB group)

No patients in the AB group reported complications after implant placement. In the NB group, two complications reported in two patients were considered as being minor (one inflammation and one swelling). Both complications healed thereafter without further therapy.

Follow-up examination and outcomes

Radiographic marginal bone levels

The median marginal bone level (distance between implant reference points and the first bone to implant contact) at the follow-up was 1.58 mm (Q1: 1.01 mm/Q3: 2.40 mm) in the AB group and 1.15 mm (0.50 mm/1.83 mm) in the NB group. This difference was statistically significant (p=0.0411). (Table 3).

Clinical parameters

Median PD values of the implants were 2.83 mm (Q1:2.50 mm/Q3:3.83 mm) in the AB group and 2.83 mm (Q1:2.67 mm/Q3:3.33 mm) in the NB group (Table 3). Median BOP [%] values of the implants were 0 (Q1:0/Q3:16.67) in the AB group and 0 (Q1:0/Q3:16.67) in the NB group (Table 3). Median PCR [%] values of the implants were 0 (Q1:0/Q3:16.67) in the AB group and 0 (Q1:0/Q3:0) in the NB group (Table 3). The median width of keratinized tissue of the implants was 3 mm (Q1:2 mm/Q3:4 mm) in the AB and 3 mm (Q1:1.25 mm/Q3:4 mm) in the NB group (Table 3). The median recession of the implants was 0 mm (0 mm/0.5 mm) in the AB and 0 mm (0 mm/0 mm) in the NB group (p=0.0503) (Table 3). There were no statistically significant differences between the groups.

Patient-reported outcome measures (PROMs) based on questionnaires

After primary augmentation (AB group)

Seven patients described an extraoral skin sensitivity after surgery at the donor site. In three sites, the skin sensitivity was still present at the follow-up. Moreover, three patients described intraoral sensitivity at the donor site being present at the follow-up examination.

Implant placement (both groups)

Five subjects in the AB group and five subjects in the NB group reported sensitivity at the implant site at the follow-up.

Evaluation of the surgical intervention (bone augmentation and implant placement in the AB, implant placement in the NB group) using a VAS

Median VAS for the overall rating of the surgical interventions were 9 (8/10) in the AB and 10 (8.5/10) in the NB group (Figure 1). The two other questions regarding the repetition of the surgical intervention was answered with similarly high VAS ratings (median VAS = 10; range between 5.5 to 10 (AB) and 7 to 10 (NB)). This was in line with patients recommending the surgical intervention of primary bone augmentation (median 10) and of implant placement in the NB group (10) to a family member.

Discussion

The present study assessing outcomes of implant therapy in sites with primary bone augmentation (AB) and sites with implant placement into native bone (NB) revealed: i) high implant survival rates independent of a primary bone augmentation procedure; ii) a higher marginal bone level in group NB compared to group AB; iii) 37% of patients with complications following the primary augmentation (group AB) and 16% of patients (groups NB and AB) with complications still present at the follow-up and, iv) a high satisfaction rate with implant therapy based on VAS questionnaires.

Both treatment modalities resulted in favorable clinical outcomes at a mean follow-up of 10 years. These results are in line with the literature (Raghoebar et al., 2007, Al-Nawas and Schiegnitz, 2014). In addition, the low rate of implant loss is in accordance with a recent meta-analysis (Moraschini et al., 2015) investigating the long-term success rates of dental implants. Although one implant was lost in the NB group due to peri-implant disease, no significant difference was observed between the two groups. Scientific evidence on dental implants placed in autogenous bone blocks and long-term follow-up data are scarce. According to clinical studies with 5-year, 10-year and 12-year follow-up examinations, the survival rate of implants placed in primarily augmented autogenous bone is high and similar to the present investigation (Keller et al., 1999) (Gulinelli et al., 2017) (Chappuis et al., 2017). Moreover, the survival rates are high and comparable to implants placed in native bone (Buser et al., 2002, Levin et al., 2007), which is, again, in line with the present study.

Apart from survival rates, marginal bone levels are a suitable tool to analyse the stability of the augmented or native bone surrounding dental implants. In the present study, a significantly lower marginal bone level was observed for implants placed in previously augmented bone compared to implants placed in pristine bone (higher MBL values). Marginal bone level(s) changes at implants placed in augmented autogenous bone blocks are relatively consistent (Galindo-Moreno et al., 2015, Johansson et al., 2001, Barone and Covani, 2007). In a clinical study with 68 implants and a 10-year follow-up, the treatment with intraoral autogenous bone blocks was considered to be successful, reporting a very limited marginal bone loss (0.6mm) over time (Roccuzzo et al., 2016). Absolute marginal bone levels, however, were not reported. Similar changes over time (up to 5 years) of 0.7mm were observed in a clinical study using autogenous bone grafts from the iliac crest. The marginal bone levels were similar to the present study, though, being located 2.0 to 2.3mm below the reference level (Dasmah et al., 2012). In the absence of data, comparing marginal bone levels at implant sites with or without primary bone augmentation, one might speculate on the reason for the observation of a significantly lower first bone to implant contact group AB in the present study. According to a histological study, the majority of the osteocytes of an autogenous transplant appeared not to survive and neovascularization was suggested to be often difficult (Acocella et al., 2010). Moreover, depending on the quality of the bone, altered resorption rates were reported (Spin-Neto et al., 2015). As such, a higher resorption of transplanted autogenous bone could at least in part explain the observed differences between NB and AB implants. This is supported by a clinical study, analyzing cone-beam computed tomographic data after block augmentation, demonstrating a mean volume resorption of 35–51% (Sbordone et al., 2009). Volumetric and linear changes of the augmented bone blocks were, however, not assessed in the present investigation. It has to be noted that additional to the block grafts, xenogenic bone particulate was used to fill up the spaces. According to (Hallman et al., 2001, Meloni et al., 2017) the use of xenogenic bone usually results in slower resorption rates. This stands in contrast to our results since we see a higher resorption rate in this group. The effect can be explained by the fact that only a minimum amount of xenogenic bone has been used during the surgery.

Moreover, the data suggest that both treatments perform well in terms of clinical outcome measures, such as PD, BOP, PCR and KT. This was underlined by both procedures resulting in long-term stable peri-implant tissues, even though on the level of the bone, differences exist. This is also in line with previous reports on the long-term outcomes of implant therapy with simultaneous guided bone regeneration and the observation that even in case of a lack of buccal bone, the soft tissues remained clinically stable to a high extent (Benic et al., 2012, Kuchler et al., 2016).

As expected, the surgical intervention of augmenting bone resulted in a relatively high complication rate of 37%. Various complications were observed subsequently including extra- and intraoral sensitivity, devitalization of neighbouring teeth and wound dehiscences at the donor site. Based on a systematic review (Nkenke and Neukam, 2014), patient's acceptance for chin bone harvesting was generally low due to pain and skin sensitivity. At the follow-up examination, the majority of the observed complications were not present anymore based on the present study. Interestingly, analysing patients' questionnaires, patient morbidity, even though being high immediately following surgery, appears to be transient. The overall rating of the procedure, the willingness to repeat the procedure and the likelihood to recommend the procedure were overall high and demonstrated no differences between the groups. These results have to be interpreted with some caution due to the retrospective study design and a, from a patients' point of view, biased participation in the follow-up examination. Moreover, the study should have been designed as a matched case-control study. The baseline characteristics of the two groups slightly differed. Any potential influence of these differences remain speculation, though.

Conclusions

Dental implants placed in sites augmented with autogenous bone or in native bone revealed healthy peri-implant tissues after 5-16 years. Marginal bone levels were significantly higher for implant placed in native bone. Complications following primary augmentation encompassed every third patient, but were mostly transient and did not affect long-term patient-reported outcome measures.

Acknowledgements and conflict of interest

The present study was fully funded by the Clinic for Fixed and Removable Prosthodontics and Dental Material Science, University of Zurich. The authors report no conflict of interest.

Figure legends

Table 1: Demographics and survival rates at 5-16 years

STM=Straumann Implant; BRA= Brånemark System; AB=autogenous block; NB=native bone

Table 2: Implant position

Implant positions and implant types are plotted in a tooth scheme; STM=Straumann Implant; BRA= Brånemark System Mk III TiUnite; AB=autogenous block; NB=native bone

Table 3: Radiographic and clinical parameters of implants at 5-16 years

Clinical measurements are plotted as median values with lower (Q1) and upper (Q3) quartile and means with standard deviations (SD). The p-values were calculated using mixed models for nonparametric testing (Brunner-Langer Analysis); STM=Straumann Implant; BRA= Brånemark System; AB=autogenous block; NB=native bone; PD=probing depth; BOP=bleeding on probing; PCR=plaque control record; KT=width of keratinized tissue; REC=buccal recession.

Figure 1: Patient related outcome measures at 5-16 years

Data from VAS are plotted as single values; Median values are shown as lines; Test=autogenous block; control=native bone.

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How would you rate the procedure?
(10 = best rating; 1 = worst rating)

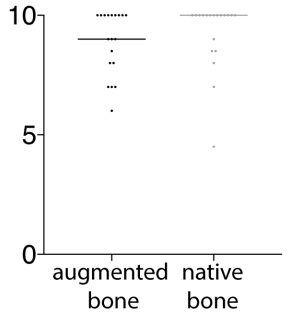

Figure 1A

Would you repeat the procedure?
(10 = best rating; 1 = worst rating)

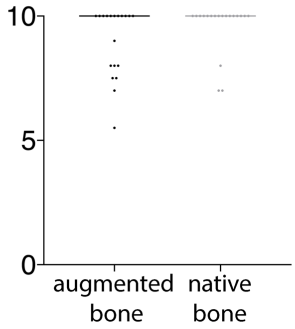

Figure 1B

Would you recommend the procedure?
(10 = best rating; 1 = worst rating)

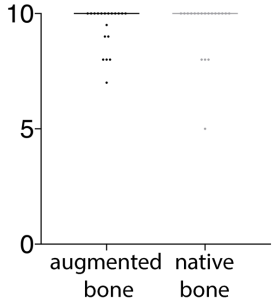

Figure 1C

Table 1

		Total	AB	NB
Age [years]		62.8	51.9	71.1
Gender	female	20	6	14
	male	18	13	5
Smoking habits	occasional smoker (5-10 cig/day)	2	2	0
	Heavy smoker (>10 cig/day)	0	0	0
	non-smoker	36	17	19
Follow-up time [years]		9.1	10.2	8.3
Number of implants		67	19	40
Implant type	STM	25	13	12
	BRA	42	14	28
Survival	number of implants	66	19	39
	%	98.5	100.0	97.5

Table 2

Site		17	16	15	14	13	12	11	21	22	23	24	25	26
AB	STM	0	0	0	0	1	3	3	1	2	1	0	0	0
	BRA	0	0	0	1	1	4	3	1	1	2	0	0	0
NB	STM	0	0	1	0	1	3	0	2	2	1	1	0	0
	BRA	0	3	2	3	2	0	2	0	2	0	2	2	1
AB	STM	0	0	0	0	0	0	1	1	0	0	0	0	0
	BRA	0	0	0	0	0	0	0	1	0	0	0	0	0
NB	STM	0	1	0	0	0	0	0	0	0	0	0	0	0
	BRA	1	1	1	0	1	0	0	0	0	1	1	1	2
Site		47	46	45	44	43	42	41	31	32	33	34	35	36

Table 3

Variable	Group	N	Mean	Std	Min	Q1	Median	Q3	Max	p-value
Marginal bone level [mm]	NB	40	1.21	0.93	0.00	0.50	1.15	1.83	3.04	
	AB	27	1.75	1.11	0.09	1.01	1.58	2.40	4.33	0.0411
PD	NB	40	3.01	0.63	1.17	2.67	2.83	3.33	4.33	
	AB	27	3.13	0.70	2.17	2.50	2.83	3.83	4.67	0.9954
BOP [%]	NB	40	7.08	10.60	0.00	0.00	0.00	16.67	33.33	
	AB	27	9.88	11.56	0.00	0.00	0.00	16.67	33.33	0.5602
PCR [%]	NB	40	4.17	8.23	0.00	0.00	0.00	0.00	33.33	
	AB	27	11.11	17.90	0.00	0.00	0.00	16.67	50.00	0.2673
KT	NB	40	2.69	1.51	0.00	1.25	3.00	4.00	6.00	
	AB	27	2.91	1.09	0.00	2.00	3.00	4.00	5.00	0.0454
REC	NB	40	0.17	0.46	0.00	0.00	0.00	0.00	2.50	
	AB	27	0.38	0.57	0.00	0.00	0.00	0.50	2.00	0.0503